



Corporate Presentation

January 2025

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Forward looking statement

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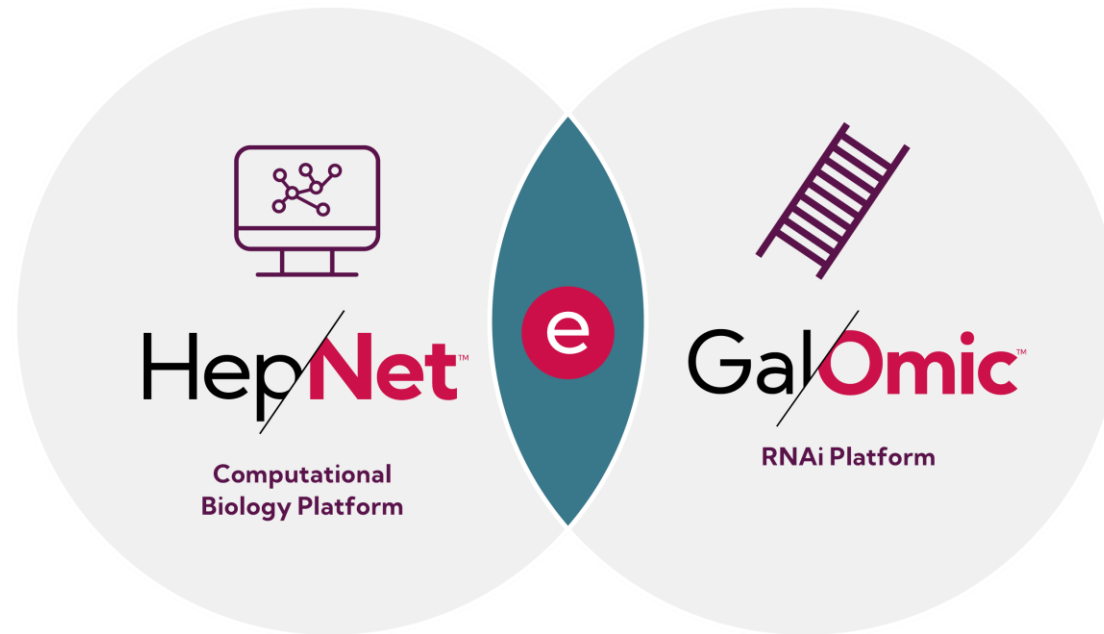
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Introduction to ETX

We leverage computation and AI to discover and develop life-transforming RNAi medicines



Uniting advanced computation and AI with RNAi, ETX accelerates the path from discovery through development and makes **better medicines faster**

We Aim To Improve Key Traditional R&D Issues

Combining computation and RNAi to revolutionise research and development

Industry Problems



**Same
Targets**



**High
Risk**



**Too
Slow**

ETX Approach

Differentiate

HepNet™ computational platform identifies novel targets with disease-modifying potential

De-risk

Lower risk of clinical failure due to extensive target-indication assessment, prioritisation of targets with genetic support, and specificity of RNAi

Deploy

Unique combination of computation and RNAi enables rapid and reproducible drug discovery and development process

GalOmic Therapies For Selective and Effective Gene Silencing

Proprietary RNAi chemistry platform enables rapid generation of potent hepatocyte-targeting siRNAs

Properties of GalOmic Therapies



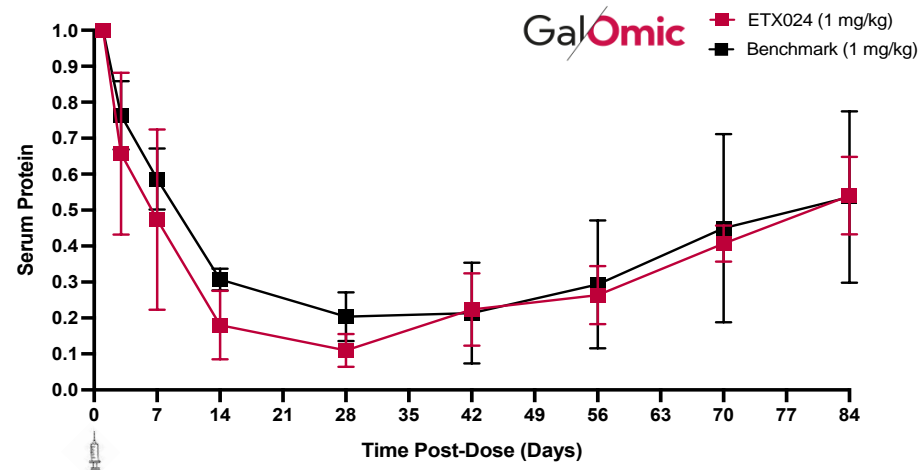
Hepatocyte-specific delivery



Highly specific silencing of target genes



Administered via subcutaneous injection



Typical performance profile of GalOmic™ constructs in non-human primate is at least equivalent to market lead across multiple genes



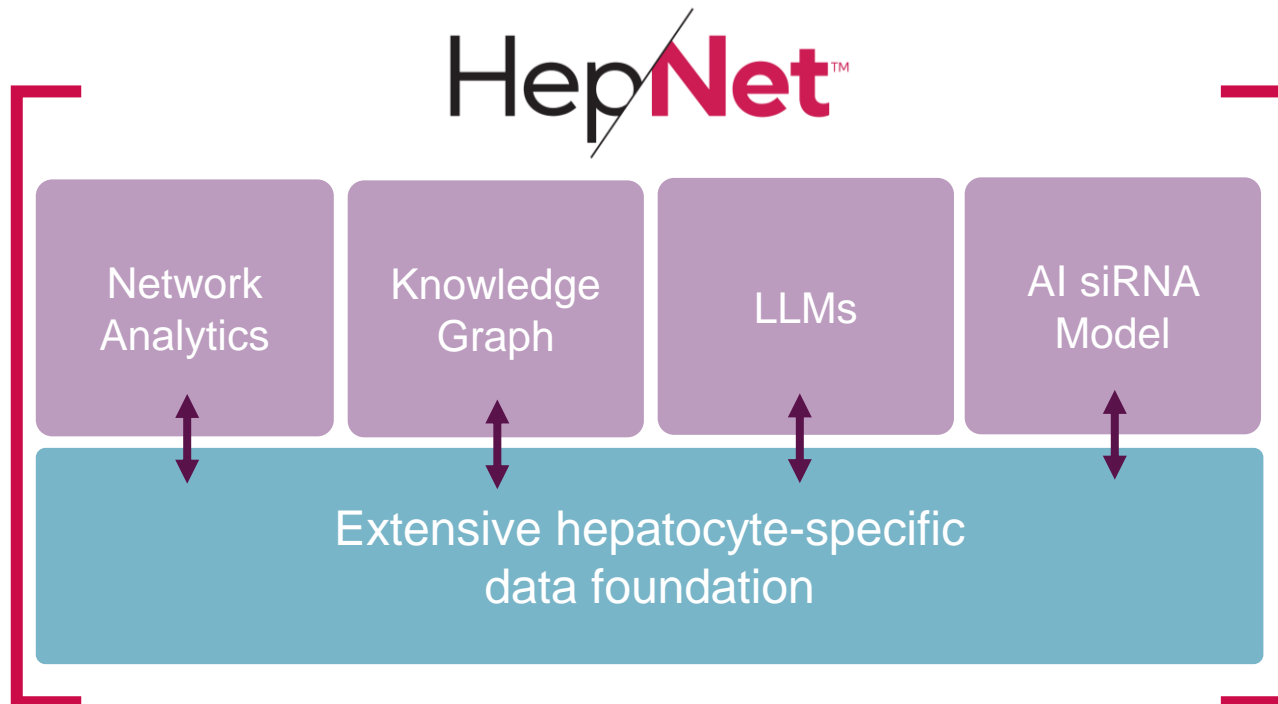
Effective, patient-friendly treatments

- **Safe** - specific gene silencing in single cell type limits unwanted side effects
- **Low treatment burden** – at least quarterly dosing regimen expected in humans (4 doses/year)
- **Low risk** - commercial-stage modality with large body of safety data and proven high probability of success in clinic



HepNet Computational Platform

Using data and AI to power discovery of GalOmic therapies

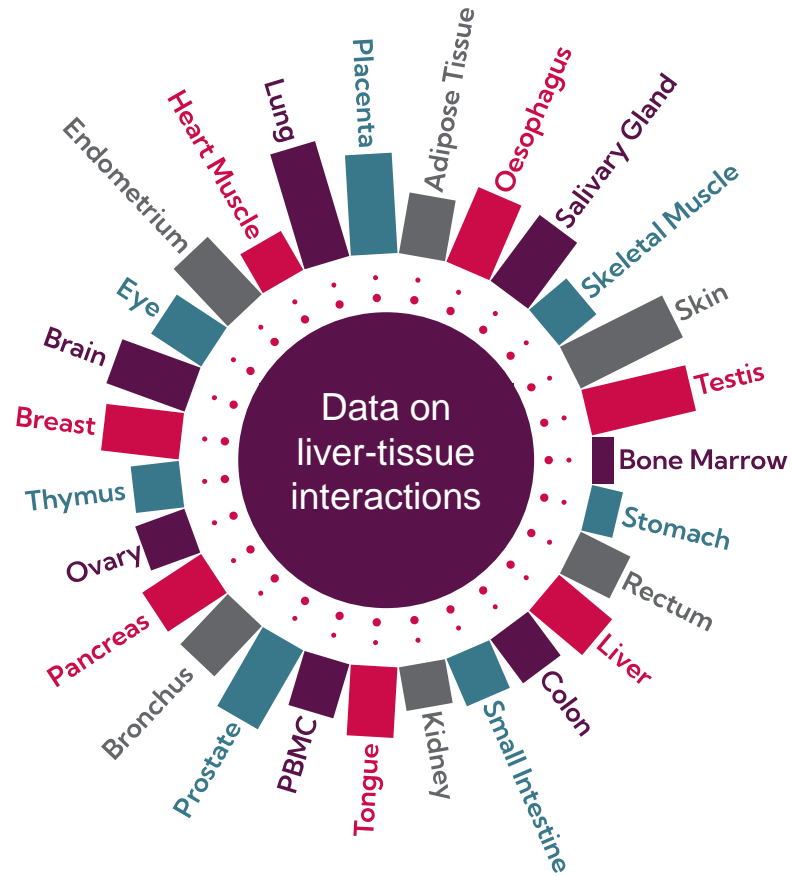


HepNet's computational approaches translate data and information into:

- Novel gene targets
- Target-indication risk scores
- Potent and long-acting siRNA sequences

Data-driven Discovery

HepNet is underpinned by our extensive hepatocyte-specific data foundation containing proprietary data and curated public and licensed data



HepNet™ knowledgebase contains:

14 million hepatocyte-specific data points

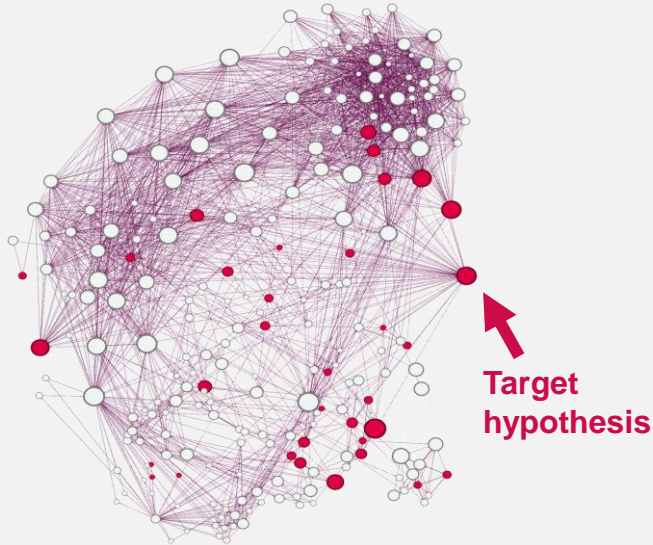
20,000 coding and non-coding genes

3,000 hepatocyte-associated diseases

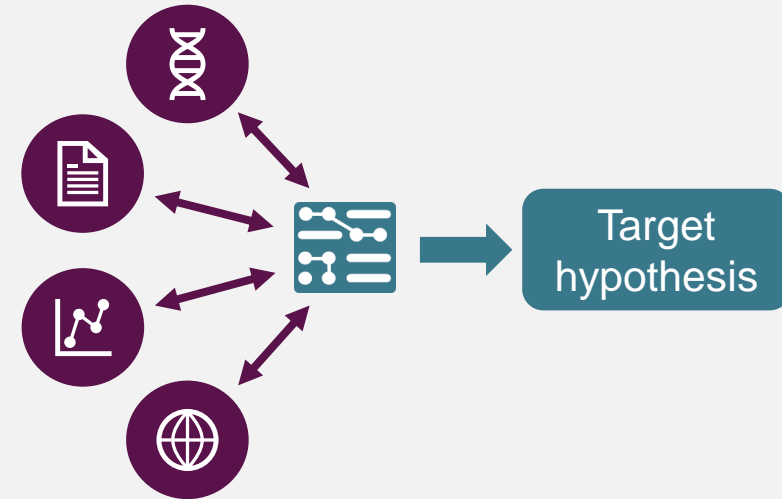
Robust data integration ensures the integrity of our computational outputs

Differentiate: Uncovering Transformational Novel Targets

HepNet's network analytics and AI approaches enhance our understanding of biology to identify high-quality targets that are not being pursued by any other RNAi company



Network analytics provide a comprehensive, holistic view of the biological systems we are targeting



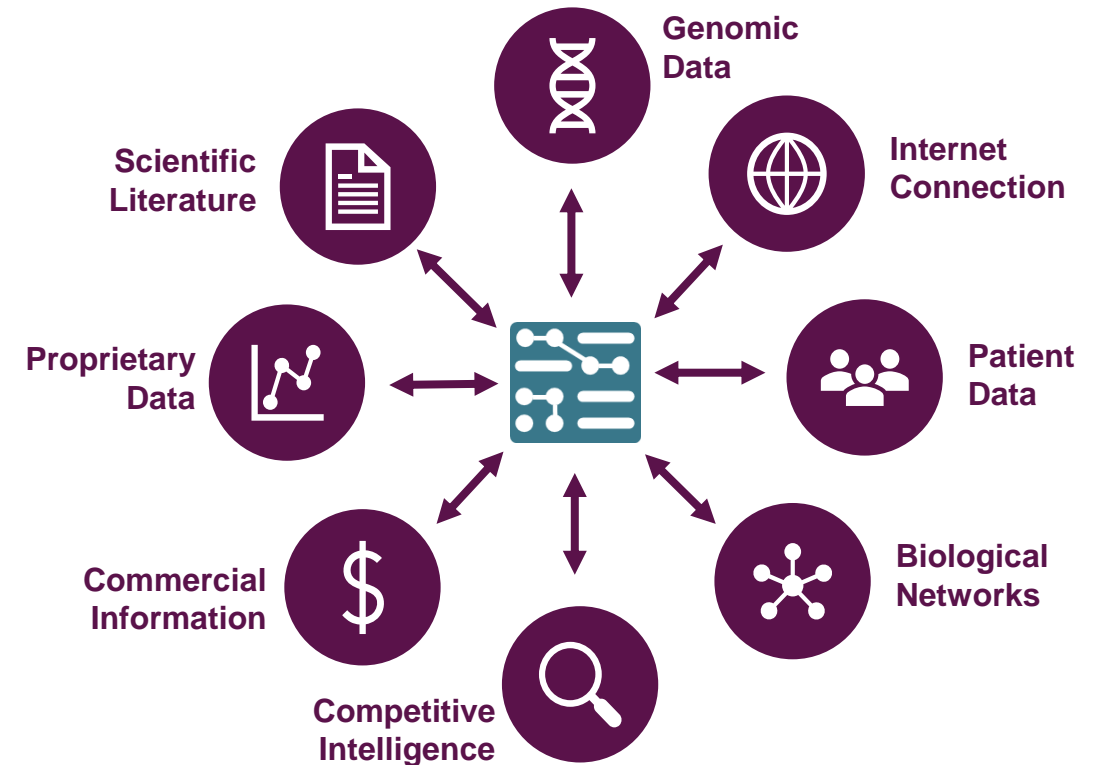
Large language models (LLMs) enhance understanding and insights from vast and disparate data sources

De-risk: Innovating with Insight

We improve probability of success by pairing RNAi and LLM-enhanced target-indication assessment

We pair our **low-risk RNAi technology** with the **right novel targets** by extensively assessing potential target-indication pairs and only **nominating high-conviction programs** to our pipeline.

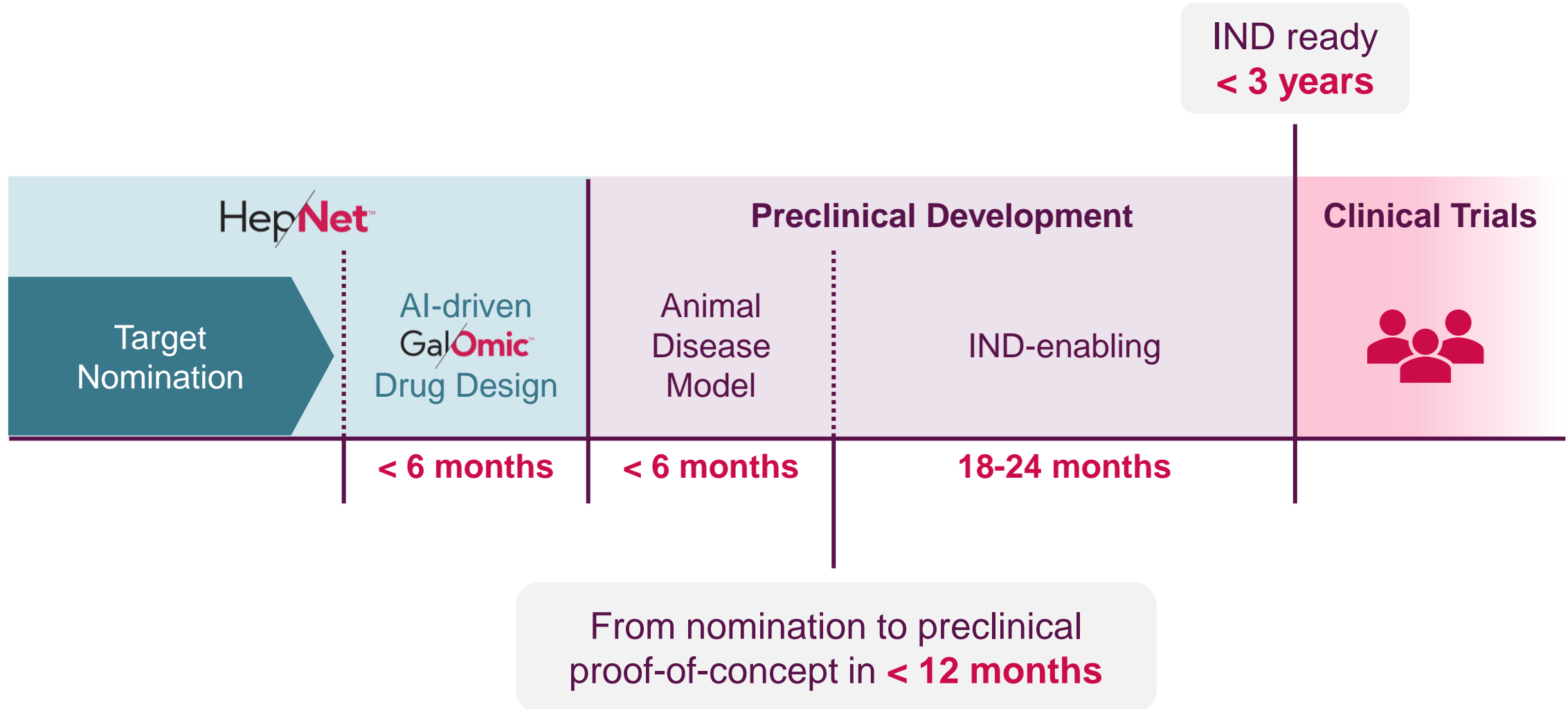
Assessment is enhanced through use of HepNet's **LLM ecosystem** to improve speed, scale, and objectivity of assessment.



LLM agent connects and infers from disparate datasets to assess a target-indication pair's biological relevance and developability and produce an objective risk score

Deploy: Our Rapid and Reproducible Process

Using the ETX approach to make better medicines faster



Computing the Future of Medicine - Today

The tangible products of our innovative approach to drug discovery

5 first-in-class GalOmic therapies in preclinical development

5 GalOmic therapies with complete preclinical proof-of-concept data

3 GalOmic therapies at IND-enabling stage

< 12 months
from target nomination to completion of preclinical proof-of-concept

Multiple
highly differentiated targets identified for in-house programs and collaborations

Competitive
depth and duration of target knockdown across GalOmic therapies









GalOmic Therapeutic Pipeline

Broad pipeline of GalOmic therapies targeting novel genes, with discovery powered by HepNet

Therapeutic Area	Program	Indication	Target ID	Drug Design	Proof-Of-Concept	IND-enabling
Liver	ETX-312 →	MASH	IND 2025			
Rare	ETX-148 →	Bleeding Disorders	IND 2026			
Immune-mediated	ETX-407 →	Dry AMD				
Cardiovascular	ETX-291 →	Cardiometabolic Disease				
	ETX-258	Heart Failure				
	Multiple targets					

A Broad Range of Opportunities

Each GalOmic therapy is a potential highly differentiated treatment for a disease with high unmet need

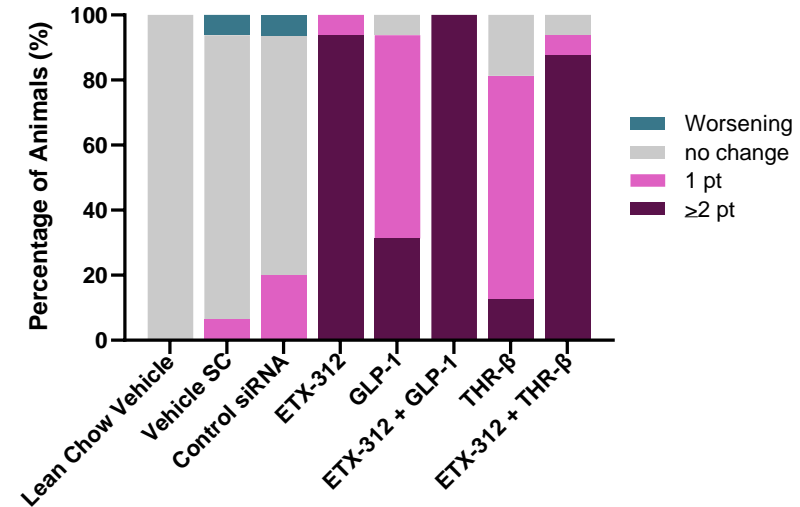
Program	Prevalence	ETX Opportunity
 ETX-312 MASH		An effective monotherapy or combination treatment with low treatment burden
 ETX-148 Haemophilia		An effective pan-haemophilia treatment with superior safety profile and low treatment burden
 ETX-407 Dry AMD		A systemic approach to treatment through subcutaneous injections
 ETX-291 Cardiometabolic Disease		Impacts wide spectrum of cardiometabolic disease drivers , resulting in more effective cardiovascular risk reduction

ETX-312 for the Treatment of MASH: From Computation to Clinic

Lead asset ETX-312 demonstrates significant therapeutic benefit in the Gubra DIO-MASH mouse model

ETX-312 computational discovery	
✓	Novel gene target identified through HepNet's network analysis of MASH
✓	siRNA sequence designed and ranked <i>in silico</i> using HepNet's AI-driven drug design model
Preclinical data includes:	
✓	Comparison and combination with THR- β agonist in DIO MASH model
✓	Comparison and combination with GLP-1 receptor agonist in DIO MASH model
Program Status	
✓	IND-enabling studies ongoing
2025	IND submission

ETX-312 Preclinical Data: NAFLD Activity Score

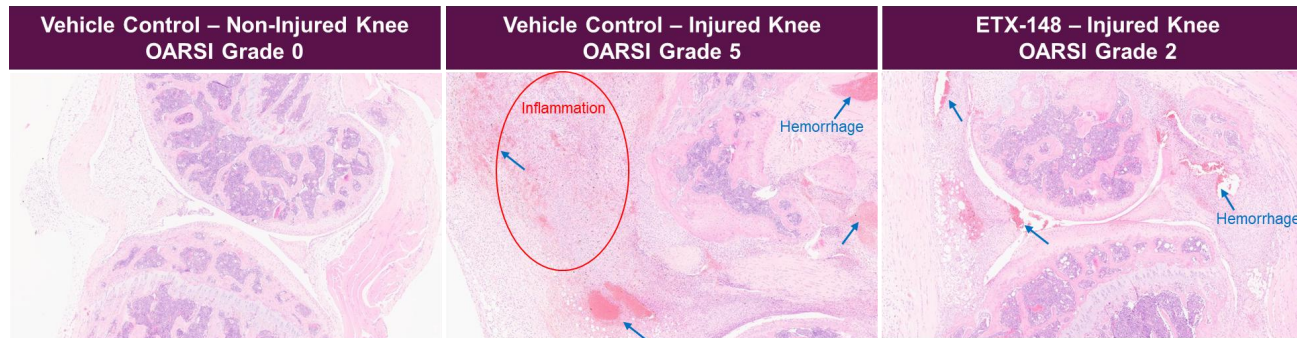


- ETX-312 **dramatically improved the NAFLD Activity Score** alone or in combination with either a GLP-1 or THR- β agonist
- ETX-312 treatment **improves liver function**
- **Significant reduction in ALT and AST levels** was observed with ETX-312 treatment alone or in combination

ETX-148 for the Treatment of Haemophilia: From Computation to Clinic

ETX-148 is a potential safe and effective pan-haemophilia treatment with low treatment burden, emergency treatment compatibility, and the ability to prevent haemarthrosis

ETX-148 Preclinical Data: Haemarthrosis



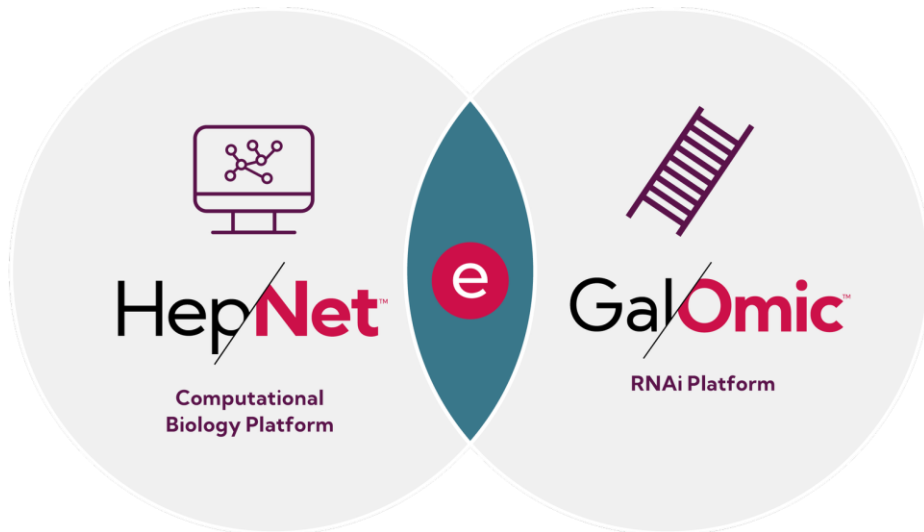
- Administration of ETX-148 resulted in **improved haemarthrosis knee joint pathology, reduced inflammation, and resulted in smaller areas of haemorrhage**
- Additional studies have demonstrated **safe administration of ETX-148 in combination with recombinant Factor therapies** in Haemophilia A & B mice (not shown)

ETX-148 computational discovery

✓	Novel gene target identified through HepNet's network analysis of coagulation pathway
✓	siRNA sequence designed and ranked in silico using HepNet's AI-driven drug design model
Preclinical data includes:	
✓	Data from animal model of haemarthrosis in haemophilia A and B
✓	Safety data alone and in combination with factor treatments or bypassing agents
Program status	
✓	Exploring expansion opportunities – studies in additional rare bleeding disorders ongoing
✓	IND-enabling studies initiated
2026	IND submission

Proven Today, Pioneering Tomorrow

Leveraging our validated cutting-edge platforms to make better medicines faster



Computing the future of medicine™
is more than a slogan,
it's our reality



Proven ability to identify novel gene targets that significantly impact diseases *in vivo*



Routinely progressing programs from target nomination to preclinical proof-of-concept in < 12 months



Advancing multiple highly-differentiated pipeline programs for broad range of diseases, with impressive success rate



Continually innovating on HepNet and GalOmic, incorporating the latest advancements in AI and RNAi chemistry

ETX Overview

Factsheet

✓ Cash runway into
2026

 **Multi-disciplinary team:**
specialists in chemistry,
computation, biology, drug
development, and AI

Locations



**London
(HQ)**



Boston

Leadership Team



Ali Mortazavi
Chief Executive
Officer



Alan Whitmore
Chief Scientific
Officer



Laura Roca-Alonso
Chief Operating &
Business Officer



**Timothy
Bretherton**
Chief Financial
Officer



Natalie Pursell
VP, Head of
Early-stage
Development



Lee Clewley
VP, Head of
Applied AI &
Informatics

Board of Directors

Lord David Prior
Non-Executive Chairman

Professor Trevor Jones CBE
Non-Executive Director

Michael Bretherton
Non-Executive Director

Jeremy Punnett
Non-Executive Director

Ali Mortazavi
Chief Executive Officer



**Computing the Future of
Medicine™**

Appendix

GalOmic™

HepNet™

ETX-312

ETX-407

ETX-148

ETX-291

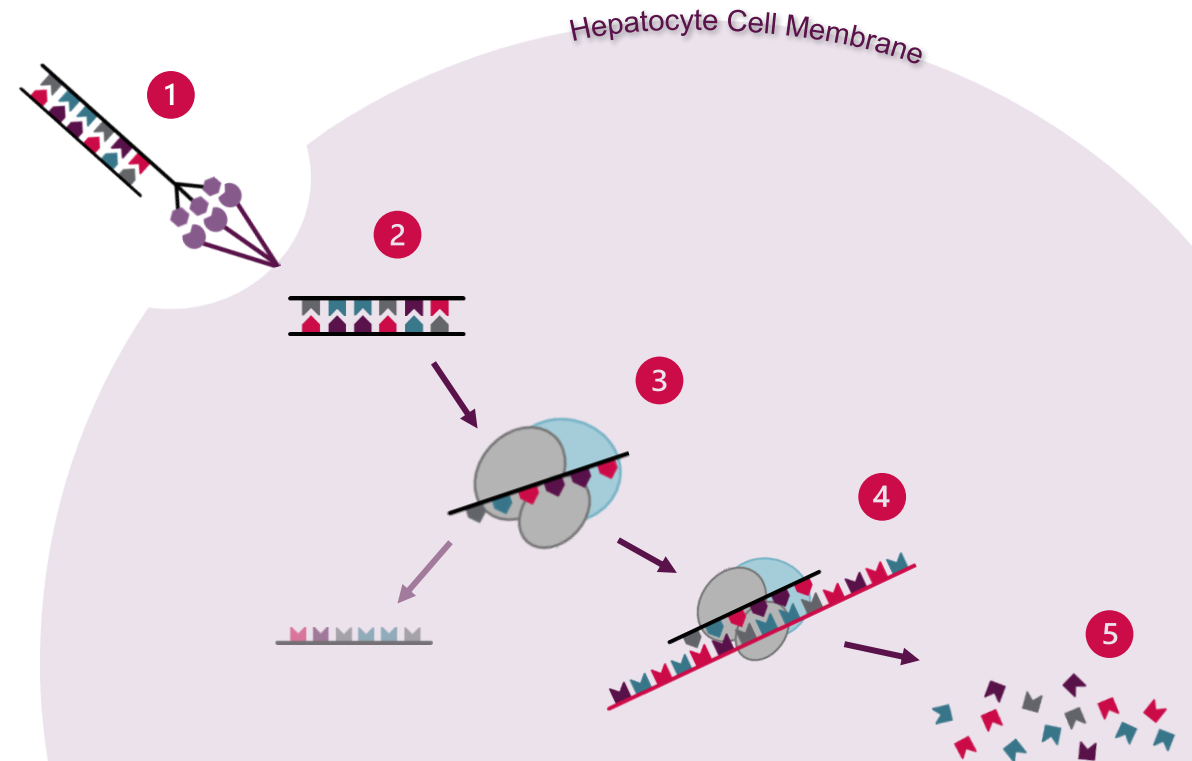
GalOmic™



Gene Silencing with GalNAc-siRNAs

Clinically validated high-precision therapeutics that can drug “undruggable” targets

- 1 GalNAc-siRNA binds to ASGPR receptor on surface of hepatocyte
- 2 siRNA enters hepatocyte
- 3 siRNA enters RNA-induced silencing complex (RISC) and unzips
- 4 RISC binds to target mRNA
- 5 Resulting in degradation of target mRNA



GalNAc - N-acetylgalactosamine | **siRNA** - small-interfering RNA |
mRNA – messenger RNA | **ASGPR** – asialoglycoprotein receptor |
RISC – RNA-induced silencing complex

GalOmic: Our RNAi Platform

Proprietary RNAi chemistry enables rapid generation of potent hepatocyte-targeting siRNAs



Hepatocyte-specific delivery



Highly specific silencing of any target gene



Administered via subcutaneous injection



Long duration of action with quarterly dosing

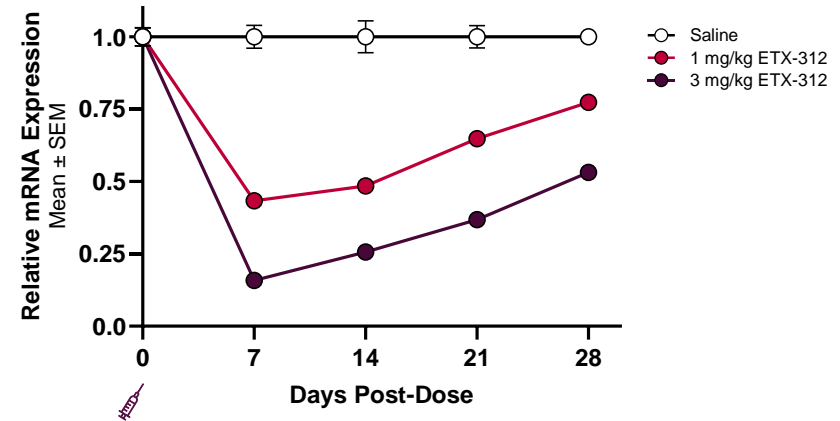


Commercial stage-modality with large body of safety data



Modality demonstrates increased probability of success in the clinic

ETX-312 Knockdown in Healthy Mice



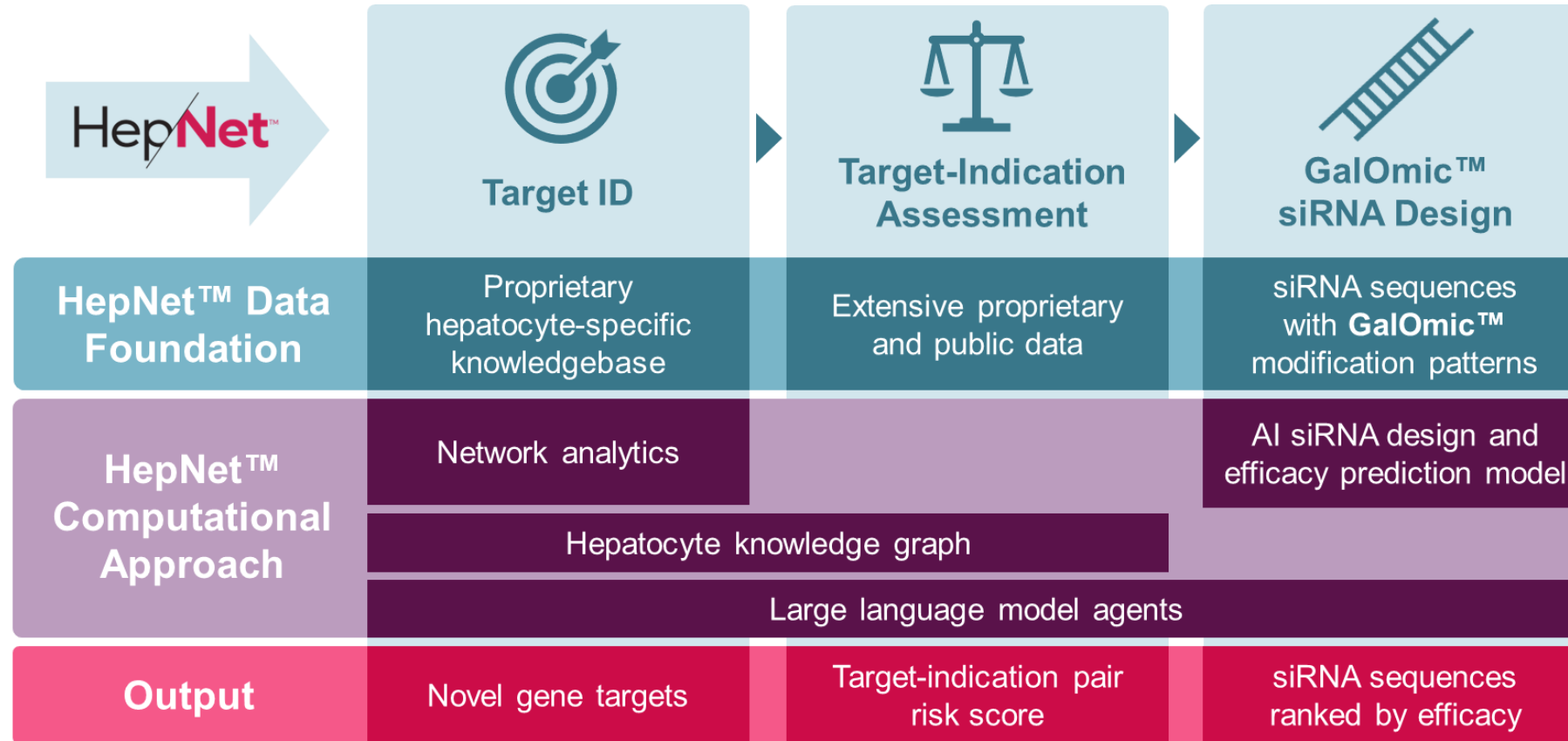
We go from target nomination to completion of preclinical proof-of-concept in **12 months**

HepNet™



Using HepNet to Differentiate, De-risk, and Deploy GalOmic Therapies

Computation and AI approaches are applied at every stage of discovery and development



We continually innovate, iterate, and improve our HepNet platform, leveraging the latest advances in computation and AI

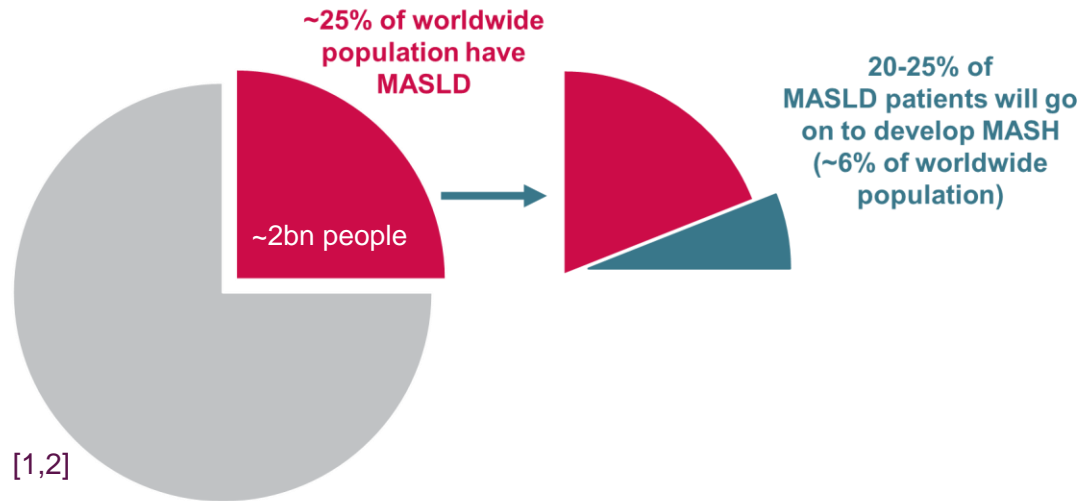
ETX-312 for the Treatment of MASH










ETX-312 for the Treatment of MASH

A safe and effective GalOmic siRNA treatment for a prevalent disease with high unmet need



Rezdiffra (THR-β agonist) is the only FDA-approved treatment and a large percentage of patients do not achieve clinically meaningful outcomes when treated with the drug.

Target Product Profile

-  **Reduced Steatohepatitis**
-  **No Worsening of Fibrosis**
-  **Improvement of MASH Biomarkers**
-  **Low Treatment Burden**
-  **Safe**

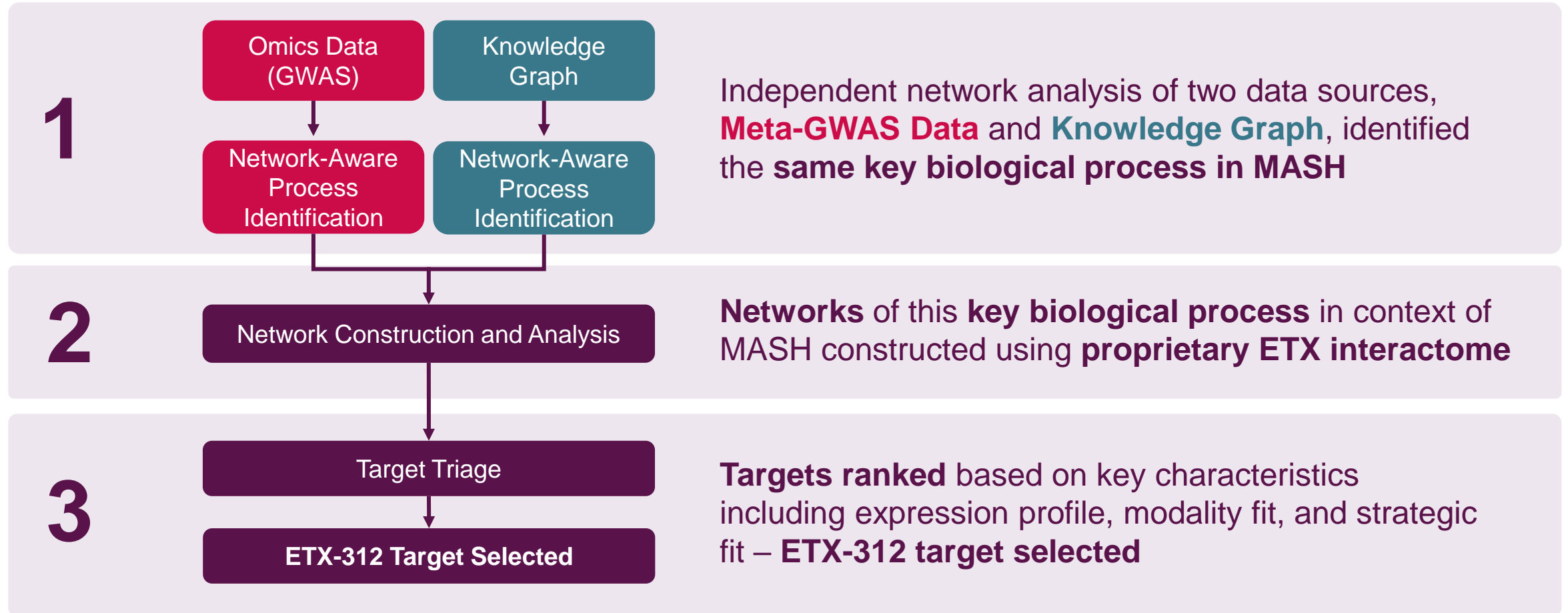
[1] Younossi, Zobair M.*; Koenig, Aaron B.; Abdelatif, Dinan; Fazel, Yousef; Henry, Linda; Wymer, Mark. Global epidemiology of nonalcoholic fatty liver disease—Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology 64(1):p 73-84, July 2016. | DOI: 10.1002/hep.28431

[2] Bellentani S. The epidemiology of non-alcoholic fatty liver disease. Liver Int. 2017 Jan;37 Suppl 1:81-84. doi: 10.1111/liv.13299. PMID: 28052624.

*MASH - metabolic dysfunction-associated steatohepatitis is now the replacement term for NASH

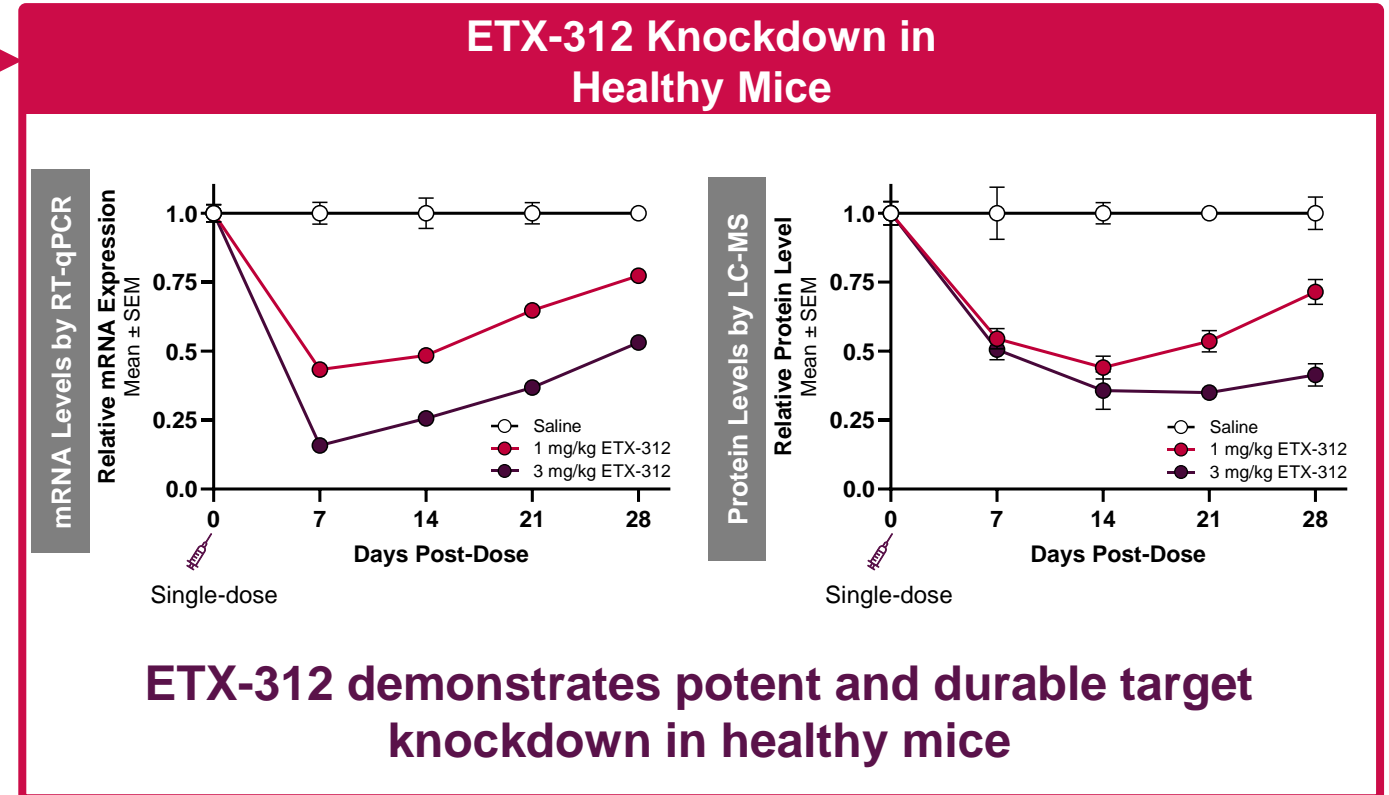
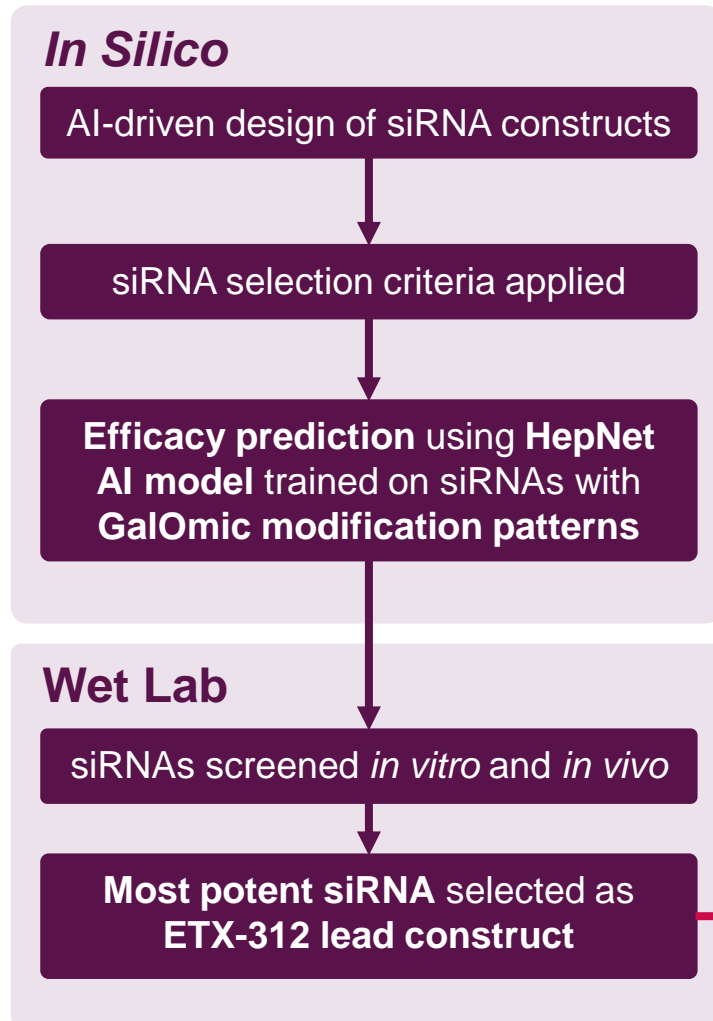
ETX-312: From Computation to Clinic

HepNet data foundation and analytical functionality deployed for target ID



ETX-312: From Computation to Clinic

Efficacy of all possible constructs ranked *in silico* using AI model trained on GalOmic siRNA chemistry

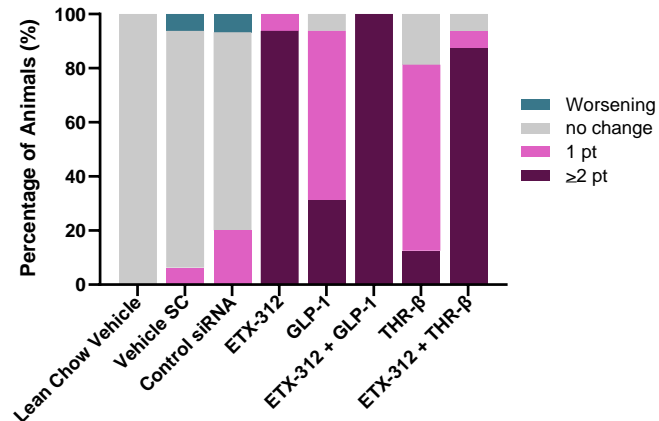
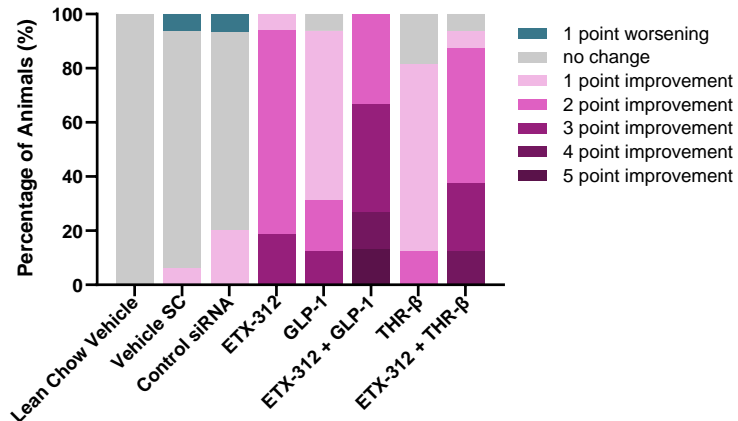




ETX-312: From Computation to Clinic

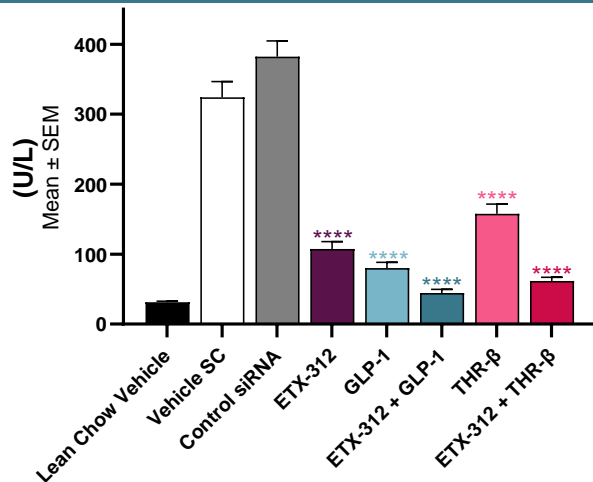
ETX-312 demonstrates significant therapeutic benefit in the Gubra DIO-MASH mouse model

NAFLD Activity Score

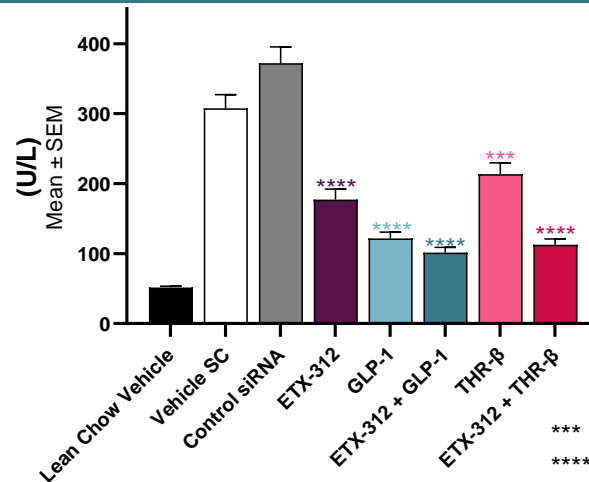


- ETX-312 **dramatically improved the NAFLD Activity Score** alone or in combination with either a GLP-1 or THR-β agonist
- ETX-312 treatment **improves liver function**
- Significant reduction in ALT and AST levels** was observed with ETX-312 treatment alone or in combination

Plasma ALT



Plasma AST



ETX-312 clinical candidate nominated and being tested in IND-enabling studies

*** p ≤ 0.001
**** p < 0.0001

ETX-407 for the Treatment of Dry AMD





ETX-407 for the Treatment of Dry AMD

Providing an effective alternative to invasive intravitreal injections



288 million people worldwide projected to have AMD by 2040 [1]



No. 1 cause of blindness in adults aged 60 yrs and older [2]

- Dry AMD **severely impacts vision and daily life** for millions – 16% of patients progress to legal blindness within two years of diagnosis. [3]
- All approved treatments for dry AMD are **intravitreally injected** – urgent need for **lower burden treatment**

Target Product Profile



Human Genetic Validation



Precision Medicine Approach



Effective Target Inhibition



Low Treatment Burden



Safe

[1] Wong, W.L. et al. (2014) "Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis," The Lancet Global Health, 2(2), pp. e106–e116. Available at: [https://doi.org/10.1016/s2214-109x\(13\)70145-1](https://doi.org/10.1016/s2214-109x(13)70145-1).

[2] VISION 2020 Global Initiative for the Elimination of Avoidable Blindness: Action plan 2006-2011. World Health Organization, 2007. World Health Organization report called: "Global data on visual impairment 2010" (WHO/NMH/PBD/12.01)

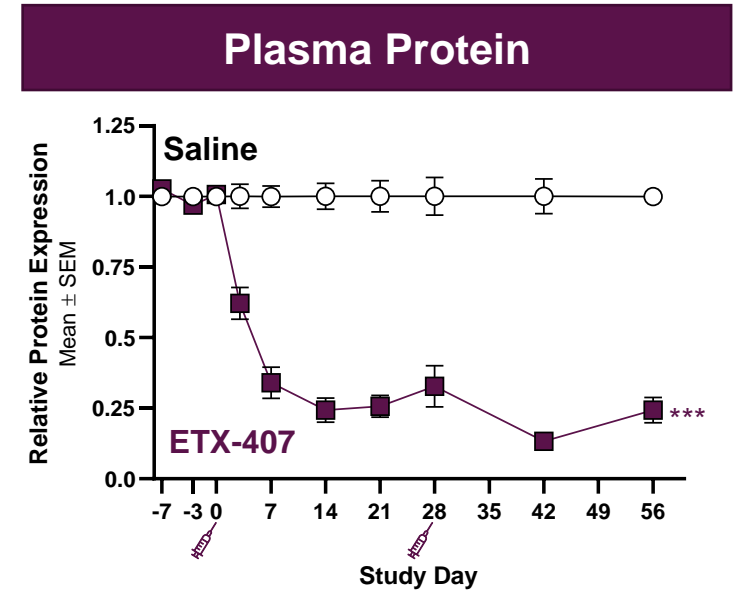
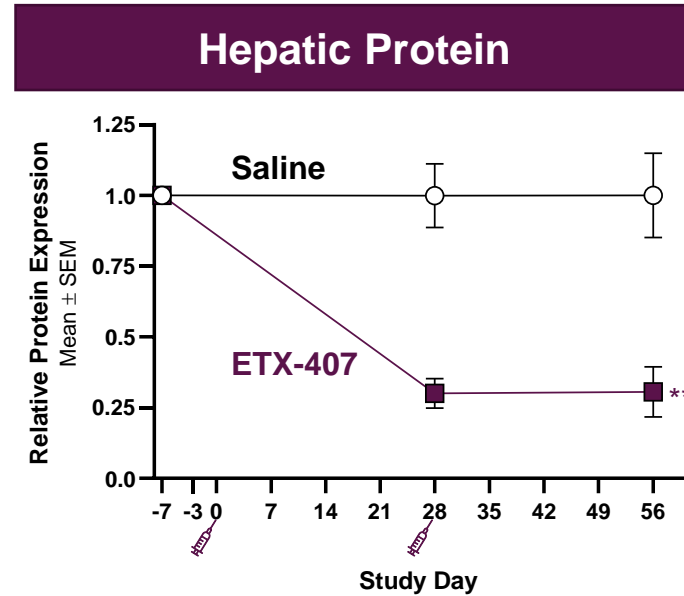
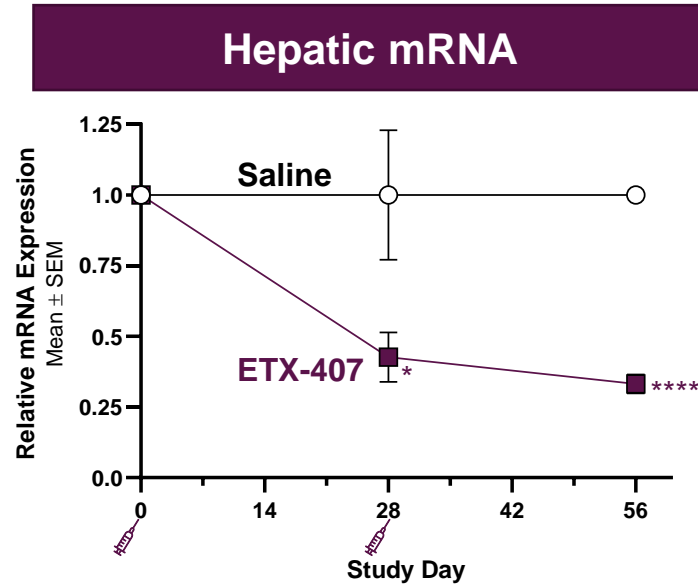
[3] Chakravarthy U, et al. (2018) Ophthalmology, 125(6):842-849.




ETX-407 Lead Candidate Selected Based on NHP Study Results

ETX-407 demonstrates the applicability of ETX's hepatocyte-targeting GalOmic platform in indications affecting distal organs

ETX-407 constructs were tested *in vivo* in *Cynomolgus macaques*



- ETX-407 effectively reduces target mRNA and protein in the liver following 1 and 2 doses (3mg/kg)
- Deep knockdown of circulating, as well as ocular, protein levels confirmed

 **ETX-407 clinical candidate nominated and proceeding to IND-enabling studies**

* p ≤ 0.05
** p ≤ 0.01
*** p ≤ 0.001
**** p < 0.0001

ETX-148 for the Treatment of Haemophilia



ETX-148: A HepNet™ Identified Pan-Haemophilia Target

Pursuing a novel pan-haemophilia rebalancing agent with good joint protection and leading safety profile



HepNet™ established link between the target and haemophilia through haemostasis network analysis



Human genetic evidence suggests reduced target expression not linked to increased risk of thrombosis unlike other rebalancing agents

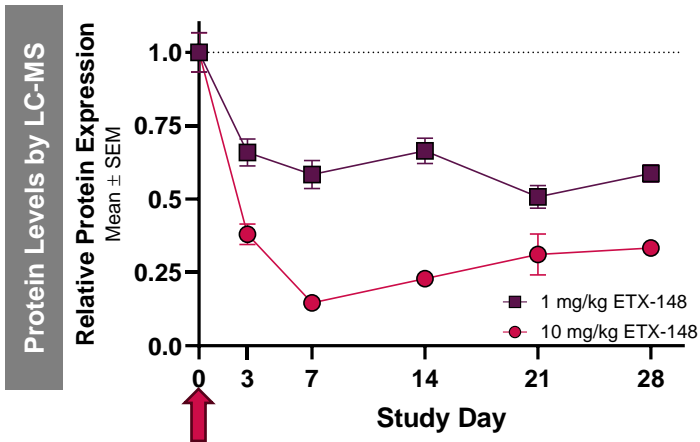
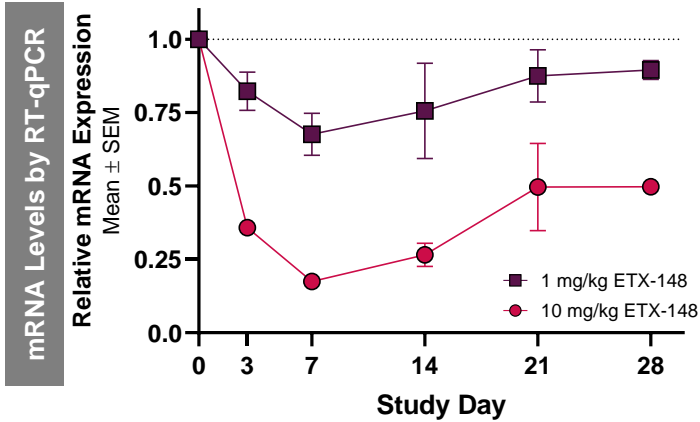
Target Product Profile

- **Combining good joint protection and a long duration of action** (aiming for quarterly+ duration)
- **Safe in combination with Factor replacement** (for emergency use)
- **Patient-friendly** subcutaneous administration
- Using ETX's proprietary **GalOmic™ GaINAc-siRNA** technology

ETX-148 is a Potent siRNA That Demonstrates Joint Protective Effects in a Haemophilia A Haemarthrosis Mouse Model

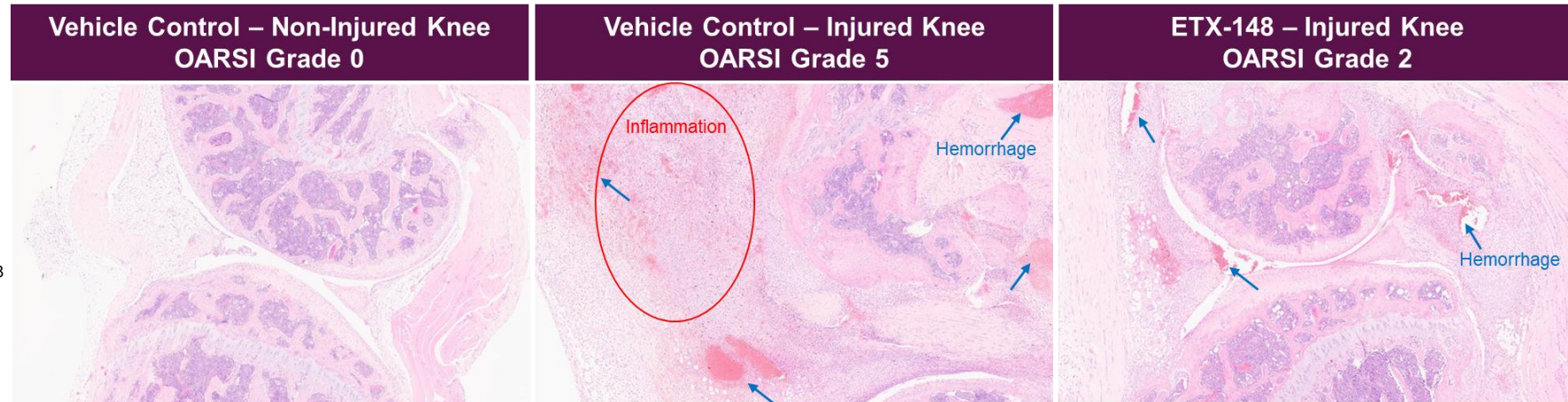


ETX-148 Knockdown in Healthy Mice



Data normalised to saline-treated mice on Study Day 0

A Haemarthrosis Study in Haemophilia A Mice



- Administration of ETX-148 resulted in improved haemarthrosis knee joint pathology, reduced inflammation, and resulted in smaller areas of haemorrhage
- Additional studies have demonstrated safe administration of ETX-148 in combination with Factor Replacement in Haemophilia A mice (not shown)

ETX-291 for the Treatment of Cardiometabolic Disease



ETX-291: A HepNet™ Identified Target for CVD Risk

Pursuing a novel target with human validation and mechanism of action beyond LDL-C modulation



HepNet™ predicted link between the target and metabolic disease risk



Human genetic evidence links target to reduced cardiovascular disease risk in otherwise healthy individuals

Target Product Profile:

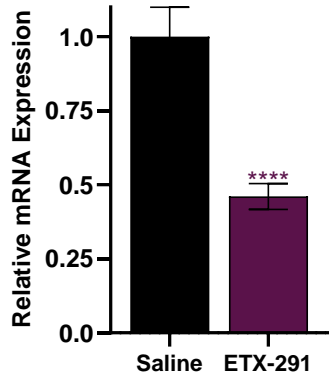
- **Meaningful CVD risk reduction** independent of statins and PCSK9s
- **Holistic treatment potential** for metabolic co-morbidities by modulating insulin sensitivity, promising applicability beyond LDL-C modulation
- Ease of use: **long-acting**, aiming for quarterly+ duration of action
- Using ETX's **GalOmic™ GaINAc-siRNA** technology for highly specific liver targeting

Pleiotropic Effects of ETX-291 on Key Cardiometabolic Risk Factors

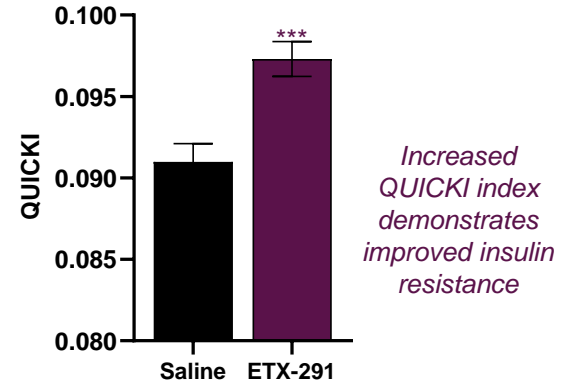
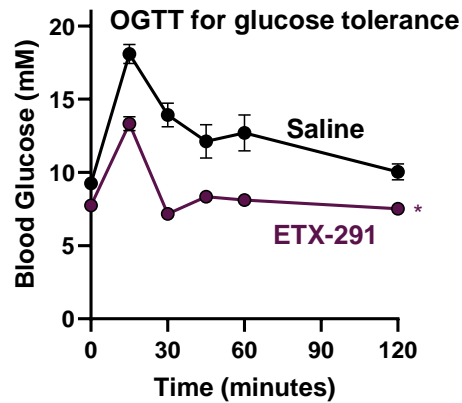


Results from a 12-week study in an ApoE*3L.CETP mouse model of metabolic syndrome

Reduced target mRNA expression

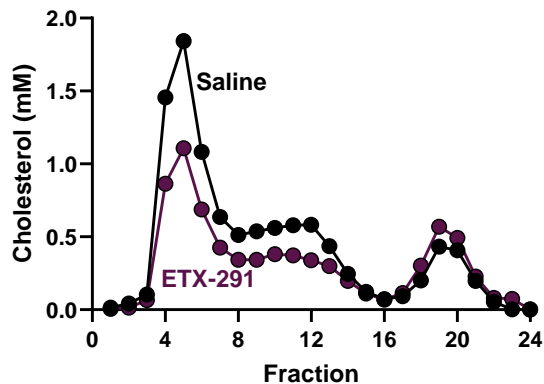


Improved glucose tolerance and insulin sensitivity

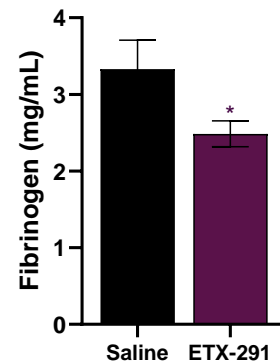


Treatment with ETX-291 provides a holistic treatment potential for cardiometabolic diseases beyond LDL-C modulation

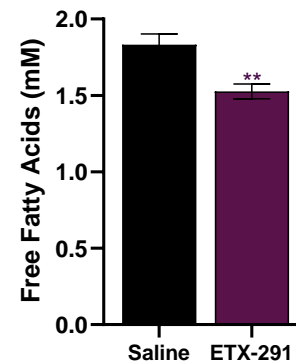
Reduced plasma cholesterol



Reduced fibrinogen



Reduced FFA



12-week study with weekly subcutaneous 10 mg/kg dose of ETX-291. Error bars: mean \pm SEM

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$